

Radiation dose and duration in coronary angiography: Driving inflammation in acute coronary syndrome patients?

Radiation dose and coronary angiography

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Abstract

Aim: Coronary angiography, a vital diagnostic and therapeutic procedure for patients with acute coronary syndrome (ACS), involves radiation exposure. This radiation exposure has the potential to trigger an inflammatory response, which may negatively impact clinical outcomes. This study investigated the relationship between radiation exposure, as measured by cumulative air kerma (CAK) and duration, and inflammatory markers during coronary angiography.

Materials and Methods: This retrospective study included 230 patients who underwent coronary angiography for suspected ACS. Demographic characteristics, medical history, and angiographic findings were recorded. C-reactive protein (CRP) and white blood cell (WBC) levels were measured before and after the procedure. Radiation exposure was recorded as CAK and duration using the fluoroscopy system.

Results: The mean age of the patients was 63.82 ± 12.64 years, and 70.6% were male. A statistically significant positive correlation was found between radiation dose (CAK) and duration, and post-procedure CRP and WBC levels ($p < 0.05$). For instance, patients with higher CAK values had significantly increased post-procedure CRP and WBC levels.

Discussion: Radiation exposure during coronary angiography can trigger an inflammatory response, potentially leading to prolonged hospital stays and an increased risk of infection. Therefore, it is crucial to minimize radiation exposure, particularly in high-risk patients (e.g., elderly, diabetic). This can be achieved through careful pre-procedural planning, implementation of radiation reduction protocols, and the use of experienced operators. Future studies should investigate protective strategies to mitigate the impact of radiation on the inflammatory response.

Keywords

coronary artery angiography, radiation exposure, systemic inflammation, acute coronary syndrome, C-reactive Protein, white blood cells

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Introduction

Acute coronary syndrome (ACS), a constellation of clinical presentations including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina pectoris, represents a spectrum of acute myocardial ischemia resulting from a sudden reduction in coronary blood flow [1]. This abrupt cessation of adequate perfusion to the myocardium triggers a cascade of pathophysiological events, culminating in myocardial necrosis and potentially life-threatening complications [2]. Despite advances in medical management and interventional cardiology, ACS remains a leading cause of morbidity and mortality worldwide, underscoring the urgent need for continued research into its underlying mechanisms and innovative therapeutic approaches [3].

The etiopathogenesis of ACS is complex and multifaceted, involving an intricate interplay of traditional risk factors such as hyperlipidemia, hypertension, diabetes mellitus, and smoking, in conjunction with emerging contributors such as inflammation and endothelial dysfunction [4]. While the occlusion of a coronary artery by atherosclerotic plaque rupture or erosion is the hallmark of ACS, recent investigations have elucidated the pivotal role of inflammation in all stages of atherosclerotic plaque development, from its initiation to its eventual destabilization and rupture [5].

Inflammatory cells, including macrophages and lymphocytes, infiltrate the arterial wall, releasing many cytokines, chemokines, and reactive oxygen species that perpetuate a chronic inflammatory state [6]. This inflammatory milieu promotes endothelial dysfunction, lipid oxidation, and smooth muscle cell proliferation, ultimately contributing to plaque growth and vulnerability. Furthermore, inflammatory mediators can trigger platelet activation and the coagulation cascade, leading to thrombus formation and acute coronary occlusion [7].

C-reactive protein (CRP), an acute-phase reactant synthesized by the liver in response to inflammation, has emerged as a sensitive biomarker of systemic inflammation and cardiovascular risk. Elevated CRP levels have been associated with increased risk of ACS, adverse cardiac events, and mortality in various patient populations. Moreover, CRP may play a direct role in atherogenesis by promoting endothelial dysfunction, monocyte adhesion, and foam cell formation [8,9].

Coronary angiography, an invasive imaging modality that visualizes the coronary arteries, is indispensable in diagnosing and managing ACS. It enables identifying culprit lesions, assessing coronary anatomy, and guiding percutaneous coronary interventions [10]. However, this procedure entails exposure to ionizing radiation, which can induce DNA damage, oxidative stress, and cellular injury. The cumulative air kerma (CAK), measured in milligrays (mGy), quantifies the radiation dose delivered to the patient during fluoroscopy and is a critical parameter in assessing radiation risk [11,12].

Several studies have suggested a potential association between radiation exposure during coronary angiography and adverse outcomes, including increased risk of restenosis, myocardial infarction, and mortality [13,14]. The underlying mechanisms involve radiation-induced inflammation and oxidative stress,

which may promote atherogenesis, thrombosis, and vascular remodeling [15,16]. However, the precise relationship between radiation dose and inflammatory response in ACS patients must still be better understood.

This study investigates the relationship between radiation dose and duration measured by CAK and inflammatory markers (especially CRP and WBC count) in coronary angiography patients due to ACS. A better understanding of this relationship may help to evaluate the possible effect of radiation exposure on the inflammatory response in this patient group. The findings may contribute to strategies to minimize radiation exposure and reduce possible side effects, thus improving ACS patients' treatment and care processes.

Materials and Methods

Study Design and Population

This retrospective observational study was conducted at the Erzurum City Hospital Cardiology Clinic. The study population consisted of 230 adult patients (age > 18 years) who underwent coronary angiography for suspected acute coronary syndrome (ACS) between January 1, 2022, and April 1, 2022. Data from these patients were accessed after ethics committee approval on July 10, 2022. No information that could identify individual participants was accessed during or after data collection. The diagnosis of ACS was established based on clinical presentation, electrocardiographic findings, and cardiac biomarker levels, specifically including patients with ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI). ACS was diagnosed according to the criteria set out in the 2023 ESC Guidelines for managing acute coronary syndromes of the European Society of Cardiology (ESC). The primary endpoint of this study was to evaluate the correlation between radiation dose and duration and inflammatory markers.

Inclusion and Exclusion Criteria

Patients were included in the study if they met the following criteria: (Figure 1).

Age Over 18 Years

Diagnosis of ACS (STEMI or NSTEMI)

Availability of complete pre- and post-procedure laboratory data in the hospital's electronic medical record system, including:

- o Hemogram (leukocyte count, platelet count)
- o Biochemistry panel
- o C-reactive protein (CRP) levels

Patients Were Excluded From the Study If They Had:

A History of Malignancy

Incomplete or Missing Laboratory Data

Prior radiation exposure: Any significant radiation exposure within the past 6 months, including radiotherapy, nuclear medicine scans, or repeated diagnostic imaging procedures, to avoid confounding effects on inflammatory markers.

Active Infection or Inflammatory Conditions

Chronic inflammatory diseases: Pre-existing chronic inflammatory diseases, such as rheumatoid arthritis, inflammatory bowel disease, or systemic lupus erythematosus, could influence baseline and post-procedure inflammatory marker levels.

Use of Anti-inflammatory Medications

Hematological disorders: Any hematological disorders

affecting leukocyte counts, such as leukemia, lymphoma, or myeloproliferative neoplasms.

Renal or hepatic impairment: Significant renal or hepatic impairment, as these conditions can affect CRP levels and other inflammatory markers.

Pregnancy or Lactation

Data Collection

Demographic data, medical history, and angiographic findings were extracted from the electronic medical records. Laboratory data, including CRP and leukocyte levels, were collected at two time points:

Pre-procedure: At the time of admission to the catheterization laboratory

Post-procedure: In the coronary intensive care unit after the procedure

Radiation exposure data were obtained from the Siemens Artis Q fluoroscopy device used for coronary angiography. The following parameters were recorded for each patient:

Cumulative air kerma (CAK), measured in milligrays (mGy), Procedure duration

Statistical Analysis

Categorical variables were summarized using frequencies and percentages. Continuous variables were assessed for normality using the Kolmogorov-Smirnov test. Normally distributed continuous variables were presented as mean ± standard deviation (SD), while non-normally distributed variables were presented as median (interquartile range [IQR]). The association between radiation exposure (CAK and procedure time) and inflammatory markers (CRP and WBC levels) was evaluated using Spearman's rank correlation coefficient. All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 23.0. Statistical significance was defined as a two-sided p-value of <0.05.

Ethical Approval

This study was approved by the Ethics Committee of Erzurum City Hospital (Date: 2022-07-04, No: 2022/09-122).

Results

Study Population

A total of 230 patients were included in this retrospective study (Figure-1). Most patients were male (70.6%), with a mean age of 63.82 ± 12.64 years (range 25-90). The prevalence of comorbidities was as follows: coronary artery disease (48.7%), hypertension (68.7%), and diabetes mellitus (40.9%). The average radiation exposure time during coronary angiography was 17.56 minutes, with an average radiation dose of 1985.04 mGy. Our study detected coronary artery disease in 118 (51.3%) of 230 patients. 58 (49.2%) of these patients underwent revascularization. 45 (77.6%) of the revascularization procedures were PCI, and 13 (22.4%) were CABG. Table 1 provides a comprehensive overview of the descriptive statistics for all variables.

Correlation Between Radiation Exposure And Inflammatory Markers WBC and Radiation Exposure:

A statistically significant, weak positive correlation was observed between radiation duration and WBC taken before the procedure (WBC-1; r=0.174, p=0.008) and WBC taken after the procedure (WBC-2; r=0.219, p=0.001). Similarly, a statistically

significant, weak positive correlation was found between radiation dose and pre-procedure WBC-1 (r=0.174, p=0.008) and post-procedure WBC-2 (r=0.202, p=0.003). No significant correlation was observed between radiation exposure (dose or duration) and WBC (WBC-2 - WBC-1) change (Table 2).

A statistically significant weak positive correlation was found between radiation duration and pre-procedure CRP (CRP-1; r=0.153, p=0.027) and post-procedure CRP (CRP-2; r=0.156, p=0.036). No significant correlation was observed between radiation dose and pre-procedure CRP-1 and post-procedure CRP-2 (Table-3).

Correlations with radiation dose and duration for WBC are

Table 1. Descriptive statistics

	Mean ± SD
Age	63.82 ± 12.64
Coronary artery disease, n (%)	112 (48.7%)
Hypertension, n (%)	158 (68.7%)
Diabetes Mellitus, n (%)	94 (40.9%)
Patients who underwent Revascularization, n (%)	58 (49.2%)
Underwent PCI, n (%)	45 (77.6%)
CABG decision, n (%)	13 (22.4%)
WAC	17.11 ± 13.81
MLGREY	2166.79 ±2031.05
WBC-1 10 ³ /mm ³	9.24 ± 3.78
WBC-2 10 ³ /mm ³	10.54 ± 4.42
Hemoglobin g/dl	13.99 ± 2.28
Platelet 10 ³ /mm ³	250.14 ± 76.35
PDW 10 ³ /mm ³	12.74 ± 7.53
Neutrophil 10 ³ /mm ³	6.94 ± 6.25
Lymphocyte 10 ³ /mm ³	1.93 ± 1.01
Monocyte 10 ³ /mm ³	0.67 ± 0.5
CRP-1 mg/dL	33.8 ± 32.1
CRP-2 mg/dL	64.7 ± 50.7

(Abbreviations: PCI: percutan coronary intervention, CABG: coronary artery bypass graft WAC: procedure time, MLGREY: radiation dose, WBC-1: white blood cell count before coronary angiography, WBC-2: white blood cell count 24 hours after coronary angiography, PDW: platelet distribution width, CRP-1: C-reactive protein level before coronary angiography, CRP-2: C-reactive protein level 24 hours after coronary angiography.)

Table 2. Examine the relationship between WBC, radiation time, and radiation dose (mGy)

	Radiation time		Radiation dose	
	r	P	r	P
WBC-1	0.174	0.008	0.174	0.008
WBC-2	0.219	0.001	0.202	0.003
WBC 2-WBC 1	0.086	0.200	0.050	0.426

(Abbreviations: r: Spearman's rho correlation coefficient, WBC: white blood cell count)

Table 3. Examination of the relationship between CRP and radiation dose and duration

	Radiation time		Raditation dose	
	r	P	r	P
CRP-1	0.153	0.027	0.094	0.176
CRP-2	0.156	0.036	0.145	0.05

(Abbreviations: CRP: C-reactive protein, r: Spearman's rho correlation coefficient.)

similar and statistically significant. For CRP, correlations with radiation dose appear stronger than with radiation duration. Confounders may be affecting these relationships. These include:

- Patient characteristics: Age, gender, general health, comorbidities (especially those affecting the immune system or inflammation), smoking status, genetics, etc.
- Radiation type: Different types of radiation have different biological effects.
- Time since radiation: Inflammatory responses may change over time after exposure.
- Medications: Many medications, including steroids and anti-inflammatory drugs, can affect WBC and CRP levels.
- Infections: Infections can cause significant changes in WBC and CRP.

Graphical Representation

Scatter plots were generated to visualize the relationships

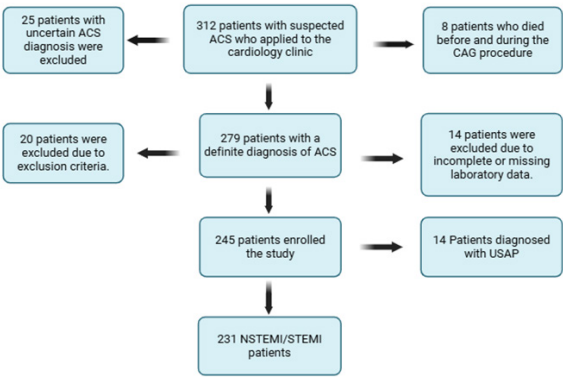


Figure 1. A flowchart of eligible individuals is included in the present study

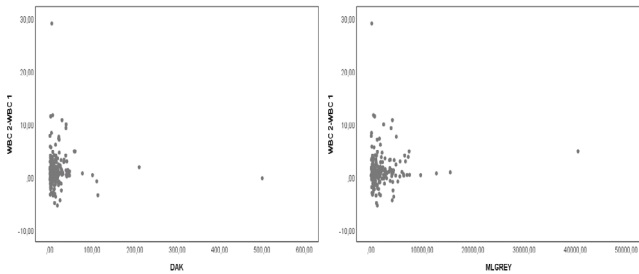


Figure 2. Scatter plot between radiation duration and dose, and WBC-2 and WBC-1 values

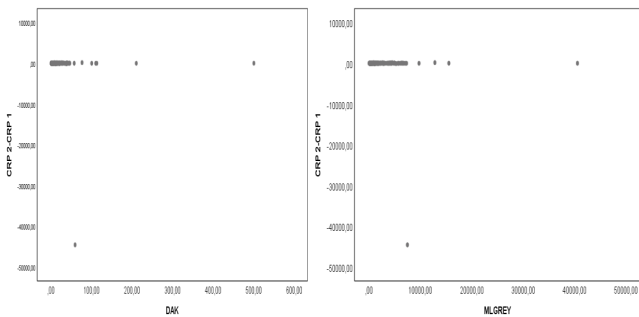


Figure 3. Scatter plots illustrating the positive correlations between radiation time and both pre-and post-procedure CRP levels

between radiation exposure (time and dose) and inflammatory markers (WBC and CRP). Figure 2 shows scatter plots showing positive correlations between radiation duration and dose and pre- and post-procedure WBC levels.

The results of this study indicate a statistically significant, albeit weak, positive correlation between radiation exposure during coronary angiography and subsequent increases in WBC and CRP levels.

Discussion

Our study provides a groundbreaking investigation into the previously unexplored association between radiation exposure during coronary angiography and subsequent inflammatory responses in patients presenting with acute coronary syndrome (ACS). The well-established detrimental effects of radiation on human health have spurred extensive research across various medical disciplines. However, the specific interaction between radiation exposure during coronary angiography and the inflammatory response in ACS patients has mainly remained uncharted.

The significant post-procedural elevation in CRP and WBC values observed in our study aligns with an emerging body of evidence linking radiation exposure to heightened inflammatory states [17,18]. Based on the potential for radiation to trigger systemic inflammatory activation via acute-phase reactants in previous studies, our findings demonstrate a clear and measurable inflammatory response even with the relatively brief radiation exposure associated with coronary angiography [19]. This observation underscores the heightened sensitivity of ACS patients to radiation-induced cellular stress and potential tissue damage.

The concurrent increase in CRP and WBC count paints a picture of a complex immune response to radiation-induced injury. While the precise molecular pathways require further elucidation, releasing damage-associated molecular patterns (DAMPs) from irradiated cells likely plays a central role. These DAMPs act as potent activators of innate immune pathways, leading to the recruitment and activation of leukocytes, thereby fueling the inflammatory cascade [20]. Considering the unique vulnerability of ACS patients in this context is imperative. The pre-existing inflammatory milieu associated with ACS, coupled with the acute physiological stress of the coronary event, may predispose these patients to exaggerated inflammatory responses following radiation exposure. The observed elevation in inflammatory biomarkers post-angiography raises concerns about potential downstream consequences. Persistent inflammation may hinder healing, prolong hospitalization, and increase susceptibility to nosocomial infections [21]. These potential complications warrant further investigation to determine the clinical implications of our findings. While our study did not include albumin assessment, the existing literature suggests a potential decline in this marker following radiation exposure [22]. Albumin, a harmful acute-phase protein, often exhibits an inverse relationship with CRP during inflammatory states [23]. Incorporating albumin measurement into future studies could provide valuable insights into the systemic effects of radiation exposure in ACS patients, potentially revealing a broader impact on protein metabolism and nutritional status.

Our study distinguishes itself from previous research by focusing on patient-specific radiation dose and its direct correlation with inflammatory markers. While prior studies have explored the effects of radiation on cardiac energy metabolism and operator safety, our findings fill a critical knowledge gap by highlighting the direct impact of radiation on the inflammatory response in ACS patients [24,25]. This novel perspective underscores the importance of minimizing radiation exposure whenever feasible, particularly in this high-risk population. This study provides an important investigation into the relationship between radiation exposure during coronary angiography and inflammatory markers. However, some limitations should be considered when interpreting the results and directing future research.

First, the study has a retrospective design, so it is impossible to draw definitive conclusions about causality. Additionally, the study was conducted at a single center, so the generalizability of the findings to other populations may be limited. The sample size was also relatively small, which may affect the study's statistical power. Finally, the study only evaluated short-term inflammatory responses. More research is needed on the long-term effects of radiation exposure and possible clinical outcomes.

Limitations

Because our study was single-center and the sample size was relatively small, the generalizability of our findings to other populations may be limited. Furthermore, our retrospective design prevents us from drawing definitive conclusions about causality.

Conclusion

Our study highlights the importance of optimizing radiation dose in patients undergoing coronary angiography, especially those with acute coronary syndromes. Minimizing unnecessary radiation exposure can reduce the risk of increased inflammation and related adverse outcomes. This may lead to reduced infection susceptibility, shorter hospital stays, and improved overall outcomes. However, these results should be evaluated within the context of the limitations of our retrospective study and need to be confirmed in prospective studies. Long-term follow-up studies, in particular, would be helpful to better assess the impact of radiation exposure on clinical outcomes. Strategies to reduce radiation dose include strict adherence to evidence-based imaging protocols, avoiding unnecessary repeat or additional projections, and having experienced operators perform the procedure. Streamlining postprocedural care and early initiation of discharge planning may also help reduce hospital stays.

In conclusion, a multifaceted approach focused on reducing radiation dose may improve coronary angiography's safety and efficacy and improve patient care. However, more research is needed in this area.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content, including study design, data collection, analysis and interpretation, writing, and some of the main line, or all of the preparation and scientific review of the contents, and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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